

514 of SEQ ID NO:3). A suitable tissue from which Kv10.1 RNA and cDNA can be isolated is nervous system tissue such as whole brain, or retina.--

Please replace the paragraph beginning at page 63, line 31, with the following:

--cDNA was prepared from either human total RNA samples or human mRNA samples using standard oligo dT priming techniques. 1/50th of each cDNA was then amplified for 35 cycles using the Kv10.1-specific primers 5'-TGGGCTGCCTGCTGCTCTTCAT-3' (SEQ ID NO:17) and 5'-CTCTCCCCTCTCCCTGCGTATGGT-3' (SEQ ID NO:18). Each cycle consisted of a denaturing step to 95°C for 20 seconds and an annealing/extension step to 63°C for 40 seconds. Amplification of Kv10.1 under these circumstances leads to the production of a 320bp fragment. Relative expression levels of Kv10.1 mRNA in the human RNA samples were determined by scoring the presence and intensity of this fragment.--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 13, at the end of the application.

REMARKS


Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the above named sequences, SEQ ID NOS:1-18, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk.

The information contained in the computer readable disk was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy. This amendment contains no new matter.

Attached hereto is a marked-up version of the changes made to the Specification by the current Amendment. The attached pages are captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,


Annette S. Parent
Reg. No. 42,058

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: (415) 576-0300
ASP:dmw
SF 1388988 v1

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Paragraph beginning at line 31 of page 6 has been amended as follows:

Figure 1: Figure 1 provides an amino acid alignment of Kv10.1 (SEQ ID NO:3) with Kv2.1 (SEQ ID NO:12) and Kv2.2 (SEQ ID NO:13). Identical amino acids are shaded, and amino acid position is given at the left margin. Gaps in the alignment are indicated by dashes.

Paragraph beginning at line 1 of page 7 has been amended as follows:

Figure 2: Figure 2 provides an amino acid alignment of the S6 domains of Kv10.1 (SEQ ID NO:14), Kv6.1 (SEQ ID NO:15) and Kv2.1 (SEQ ID NO:16). Arrows mark two residues that typically differ between normal Kv family polypeptides that form functional channels as homomultimers and electrically silent Kv channel polypeptides that form functional channels as heteromultimers. These residues are always glycine (G) and proline (P), respectively, in Kv subunits that express as homotetramers. Kv10.1 differs at these residues, much like the electrically silent subunit Kv6.1.

Paragraph beginning at line 23 of page 27 has been amended as follows:

In general, the nucleic acid sequences encoding Kv10.1 and related nucleic acid sequence homologs such as other Kv10 subfamily members are cloned from cDNA and genomic DNA libraries or isolated using amplification techniques with oligonucleotide primers. For example, Kv10.1 sequences are typically isolated from human nucleic acid (genomic or cDNA) libraries by hybridizing with a nucleic acid probe or polynucleotide, the sequence of which can be derived from SEQ ID NOS:1-2, preferably from the region encoding the conserved region (*see, e.g.*, amino acids 102 to

514 of SEQ ID NO:3-SEQ ID N3). A suitable tissue from which Kv10.1 RNA and cDNA can be isolated is nervous system tissue such as whole brain, or retina.

Paragraph beginning at line 31 of page 63 has been amended as follows:

cDNA was prepared from either human total RNA samples or human mRNA samples using standard oligo dT priming techniques. 1/50th of each cDNA was then amplified for 35 cycles using the Kv10.1-specific primers 5'-TGGGCTGCCTGCTGCTCTTCAT-3' (SEQ ID NO:17) and 5'-CTCTCCCCTCTCCCTGCGTATGGT-3' (SEQ ID NO:18). Each cycle consisted of a denaturing step to 95°C for 20 seconds and an annealing/extension step to 63°C for 40 seconds. Amplification of Kv10.1 under these circumstances leads to the production of a 320bp fragment. Relative expression levels of Kv10.1 mRNA in the human RNA samples were determined by scoring the presence and intensity of this fragment.